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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,733	05/20/2005	Osamu Ohara	1254-0282PUS1	2831

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	01/17/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 01/17/2007.

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mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/535,733	OHARA ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6-17 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *May 20, 2005 and Sept. 7, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-5 and 18-19, in the reply filed on November 17, 2006 is acknowledged. The traversal is on the ground(s) that searching all the claims would not be an undue burden for the examiner and that in the art used to provide lack of unity the biological activity of the homologous sequence was not tested or confirmed. This is not found persuasive because examination of claims containing nucleotide sequences require searching 10-15 databases while examination of claims containing protein sequences require searching 10-15 databases which differ from the nucleotide databases. Additionally, the specification of the present application does not disclose the testing or confirmation of biological activity for the protein of SEQ ID No. 2 other than homology comparisons. In addition, the claims require biological activity that is substantially equivalent to some polypeptide that is substantially identical to SEQ ID No. 2, which is unclear and as such the art teaches a peptide that is substantially identical, therefore, it would have an activity that is substantially equivalent.

The restriction requirement is still deemed proper and is therefore made FINAL.

2. Claims 6-17 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 17, 2006.

Claims 1-5 and 18-19 are under examination.

Specification

3. The use of the trademarks Matchmaker™, hybriZAP™, TNT T7™, Kaleidoscope™, ABI Prism™, TaqMan™ and Isogen™ have been noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The trademark symbols and generic terminology are not included for the above-mentioned trademarks. Appropriate correction is requested for all trademarks throughout.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a.) Claims 1 and 2 recite "biological activity substantially equivalent to the function of the polypeptide." It is not clear what is meant by biological activity

substantially equivalent, does this refer to enzymatic activity, binding activity, immunological activity, or inhibiting activity, for example.

b.) Claims 2 and 18 recite hybridizing under stringent conditions. It is unclear what is meant by stringent conditions. The specification discloses examples of stringent conditions (page 10 last paragraph), but does not disclose the specific hybridization conditions which are stringent.

c.) Claim 3 recites a gene comprising the DNA of claim 1. It is not clear what constitutes a gene. According to Genes IV (Lewin et al, Oxford University Press, page 810, 1990), a gene is defined as "the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding regions (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons)." From the teachings of the specification, however, the nucleic acid sequence appears limited to the specific coding regions, and does not include expression control elements that fall under the definition of a gene.

Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5 and 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding SEQ ID No. 2 or the DNA of

SEQ ID No.1, does not reasonably provide enablement for deletions, substitutions, additions, hybridizing DNA, complementary DNA encoding a polypeptide, or a gene comprising the polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

8. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

9. The claims are drawn to a DNA comprising a nucleotide sequence consisting of a polypeptide identical or substantially identical to SEQ ID No. 2, a DNA hybridizing under stringent conditions to a nucleotide sequence complementary to the DNA and having a biological activity substantially equivalent to the polypeptide of SEQ ID No.2. The claims are also drawn to a gene, expression vector, and transformant comprising the polypeptide of SEQ ID No. 2 and a polynucleotide that hybridizes under stringent conditions to the DNA.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol. 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol. 8 No 3 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin (Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411, 1987). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin et al Biochemistry USA Vol. 14:1559-1563,1975).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Even if one has the correct amino acid sequence, a skilled practitioner would not be able to predict the level of expression of the resulting synthetic DNA sequence. Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. Elucidation of the genetic code induces one to believe that one can readily obtain a

functional synthetic protein for any known nucleic acid sequence with predictable results. The results of the construction of synthetic proteins remain very unpredictable as Burgess et al, Lazar et al, Schwartz et al, and Lin et al conclusively demonstrate.

The specification does not disclose the sequence of the promoter elements, any upstream or downstream enhancer or suppressor elements or intron sequences which would be included in a gene as defined above by Lewin, et al., nor does the specification disclose a use for the polypeptides of SEQ ID Nos. 3 and 4 which hybridize to the DNA of SEQ ID No.1.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 1-3 and 18-19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-3 and 18-19, as written, do not sufficiently distinguish over nucleotides and polypeptides as they exists naturally because claims 1-3 and 18-19 do not particularly point out any non-naturally occurring differences between the claimed

nucleotides and polypeptides and the structure of naturally occurring nucleotides and polypeptides.

In the absence of the hand of man, the naturally occurring nucleotides and polypeptides are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" nucleotide or polypeptide or similar language would obviate this rejection.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-5 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanjanwala, et al (WO 2002/46426 A2).

The claims recite a DNA comprising a nucleotide sequence encoding the polypeptide consisting of the amino acid sequence identical or substantially identical to SEQ ID No. 2 and having a biological activity substantially equivalent to the function of the polypeptide, a gene, a vector, and a transformant comprising the DNA, and a

polynucleotide hybridizing under stringent conditions to the DNA encoding SEQ ID No.2.

Sanjanwala, et al. teach a DNA comprising a nucleotide sequence of SEQ ID No. 8 which has 86.5% homology to SEQ ID No.2 and is a drug metabolizing enzyme (see previous action). Sanjanwala, et al. also teach the recombinant polynucleotide comprising a promoter sequence and a cell transformed with the recombinant polynucleotide (see Claims 6 and 7).

Since the claims do not define the biological activity of the polypeptide and the nucleic acid does not need to be fully identical, and one would envisage that DNA having homology to the DNA encoding SEQ ID No.2 would hybridize under the claimed conditions, all the limitations of the claims have been met.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

January 3, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER